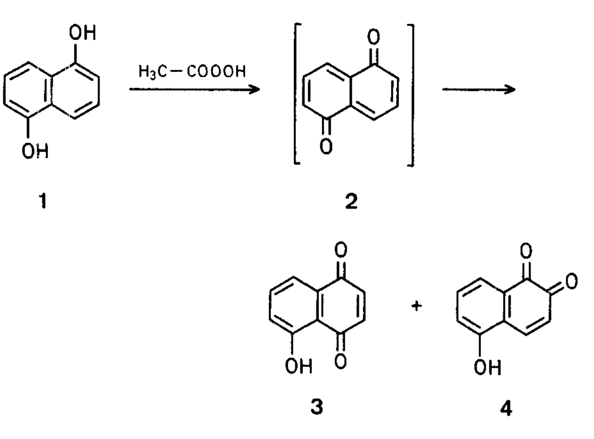
A New Synthesis of Juglone

Christoph Grundmann

Carnegie-Mellon Institute of Research, Pittsburgh, Pennsylvania 15213, U.S.A.

The preparation of juglone, 5-hydroxy-1,4-naphthoquinone (**3**), has recently gained interest because of its activity as an allelopathic agent[1-7]. None of the various known methods for the synthesis of **3** is satisfactory, either the yield is very low or the starting materials are not easily accessible[2-6]. Most frequently used has been the oxidation of 1,5-dihydroxynaphthalene (**1**) with chromic acid[3,7,8], although only a 10% yield of pure juglone is thus obtainable[9].

It was found that peracetic acid – which is known to convert 2,2'-dihydroxybiphenyl into 2-(2-hydroxyphenyl)-1,4-benzoquinone[10] – oxidizes 1,5-dihydroxynaphthalene smoothly to a mixture of juglone (**3**) and 5-hydroxy-1,2-naphthoquinone (**4**). Products **3** and **4** can be easily separated by extraction of the crude oxidation product with pentane, in which only **3** is soluble. Pure juglone is thus obtainable in about 50% yield[11]. Compounds **3** and **4** are predominantly formed if **1** is added to an excess of peracetic acid, the reverse mode of addition leads mostly to dark resins. This indicates that the first step of the oxidation is probably the dehydrogenation of **1** to the unstable 1,5-naphthoquinone (**2**) which polymerizes very rapidly. Only in presence of an excess of oxidans does subsequent hydroxylation in 4- or 8- resp. in 2- or 7-position stabilize the intermediate **2**, either as the *p*-quinone **3** or as the *o*-quinone **4**.



Consistent with this interpretation of the reaction mechanism is the fact that under the same conditions, 1,8-dihydroxynaphthalene – which cannot form a quinoid intermediate analogous to **2** – yields only resinous materials.

Oxidation of 1,5-Dihydroxynaphthalene with Peracetic Acid:
1,5-Dihydroxynaphthalene (8.0 g) is added in ~0.6 g portions in intervals of 15–20 min to a well-stirred solution of peracetic acid in acetic acid (75 g, 12.3% CH$_3$COOOH) prepared as described[10,12]. After 3 h more peracetic acid (15 g, total equiv. 2.4 mol O$_2$) is added. The reaction mixture is kept at 20–24° by occasional cooling with water and finally stirred for 1 h more. The formed deep-red slurry is distilled from a 35° water bath in vacuo to dryness and the residue (9.1 g) is extracted in a Soxhlet with pentane until the effluent is practically colorless (~72 h). During the extraction most of the juglone crystallizes out in orange red needlets, an equally pure portion is obtained by evaporation of the mother liquor; total yield: 4.00–4.35 g (46–50%); m.p. 150–154° with dec. beginning >130°; Lit.[3] m.p. 149–150°.

The pentane-insoluble part of the crude oxidation product, digested with acetic acid (20 ml), filtered, washed with little acetic acid, then with ether until the eluate is colorless, gives 5-hydroxy-1,2-naphthoquinone; yield: 2.6 g (28%); m.p. 172–176° with dec., identical with an authentic specimen[6].

When peracetic acid (66 g, 12.3%, equiv. to 2.1 mol O$_2$) is added dropwise under the conditions described above to 1,5-dihydroxynaphthalene (8.0 g) dissolved in ethyl acetate (200 ml), only very impure juglone (472 mg, 5.4%) could be isolated.

Received: May 9, 1977

---

[1] H. R. Bode, *Planta* **51**, 440 (1958).
E. Sondheimer, J. B. Simeone, Eds., *Chemical Ecology*, Academic Press, New York, 1970.

[2] F. Mylius, *Ber. Dtsch. Chem. Ges.* **17**, 2411 (1884); **18**, 463 (1885): oxidation of 1,4,5-trihydroxynaphthalene with bromine or iron(III) chloride.

[3] R. Willstätter, A. S. Wheeler, *Ber. Dtsch. Chem. Ges.* **47**, 2796 (1914): oxidation of 1,5-dihydroxynaphthalene with chromic acid or lead(IV) oxide, oxidation of 4-amino-1,5-dihydroxynaphthalene with iron(III) chloride.

[4] P. Friedländer, L. Silberstern, *Monatsh. Chem.* **23**, 513 (1902): oxidation of 1,4-diamino-5-hydroxynaphthalene with iron(III) chloride.

[5] H. Goldstein, P. Grandjean, *Helv. Chim. Acta* **26**, 181 (1943): oxidation of 4-amino-1,5-dihydroxynaphthalene with iron(III) chloride.

[6] H. Teuber, H. Götz, *Chem. Ber.* **87**, 1236 (1954).
F. A. Richey et al., *J. Agr. Food Chem.* **20**, 825 (1972): oxidation of 1,5-dihydroxynaphthalene with dipotassium nitrosodisulfonate.

[7] A. Bernthsen, A. Semper, *Ber. Dtsch. Chem. Ges.* **20**, 934 (1887).
L. F. Fieser, J. T. Dunn, *J. Am. Chem. Soc.* **59**, 1016 (1937).

[8] G. Jesaitis, A. Krantz, *J. Chem. Ed.* **49**, 436 (1972).

[9] Higher yields reported in earlier literature refer apparently to a rather crude product.

[10] C. Grundmann, *Ber. Dtsch. Chem. Ges.* **69**, 1755 (1936).

[11] After this work was completed, J. Griffiths, K.-Y. Chu, C. Hawkins (*J. Chem. Soc. Chem. Commun.* **1976**, 679) have claimed the photo-sensitized air oxidation of 1-naphthol to be "the most convenient route to juglone". This statement is true with regard to starting material, oxidans, and yield (70%), but as a synthetic method their process is impractical for the preparation of more than about 1 g quantities of **3** because of the necessity to work at a very high (10^{-2} molar) dilution.

[12] It is essential that the peracetic acid is distilled in vacuo: in presence of the catalytic amounts of sulfuric acid used in its preparation the yield of juglone is very low. Likewise, mixtures of hydrogen peroxide and acetic acid do not oxidize 1,5-dihydroxynaphthalene to juglone.